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NEW TYPES OF AMINATION OF OLEFINIC,ACETYLENIC AND AROMATIC COMPOUNDS BY HYDROXYLAMINE-O-SULFONIC ACID AND HYDROXYLAMINES/ METAL SALTS REDOX SYSTEMS.

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IN recent syntheses with N-chloroamines we[1] have postulated amino radicals as intermediates in the redox system:

$$R_2N\text{-}Cl \;+\; M^+ \longrightarrow R_2N\cdot \;+\; MCl^+$$

From the known analogy between N-chloroamines and hydroxylamine-O-sulfonic acid we have been induced to investigate the reaction of this acid in the presence of several organic substrata in order to verify the possible interaction:

$$H_2NOSO_3H \;+\; Fe^{++} \longrightarrow \cdot NH_3^+ \;+\; SO_4^{--} \;+\; Fe^{+++}$$

Actually in the decomposition of H_2NOSO_3H with $FeCl_2$ in the presence of olefins such as styrene,1-hexene and cyclohexene we have obtained the aminochlorination of the olefin in 25-45% yield.This result is in accordance with the attack of the amino radical to the double bond and the oxidation of the alkyl radical by a ligand transfer process:

$$\cdot NH_3^+ \;+\; \overset{|}{\underset{|}{C}}{=}\overset{|}{\underset{|}{C}} \longrightarrow NH_3^+\text{-}\overset{|}{\underset{|}{C}}\text{-}\overset{|}{\underset{|}{C}}\cdot$$

$$NH_3^+\text{-}\overset{|}{\underset{|}{C}}\text{-}\overset{|}{\underset{|}{C}}\cdot \;+\; FeCl^{++} \longrightarrow NH_3^+\text{-}\overset{|}{\underset{|}{C}}\text{-}\overset{|}{\underset{|}{C}}\text{-}Cl \;+\; Fe^{++}$$

If the addition to styrene is carried out in methanolic solution with $FeSO_4$,instead of $FeCl_2$,an aminoether is produced:this could be the result of an electron transfer oxidation of the benzylic radical:

$$C_6H_5\text{-}\overset{\bullet}{C}H\text{-}CH_2\text{-}NH_2 \;+\; Fe^{+++} \longrightarrow C_6H_5\text{-}\overset{+}{C}H\text{-}CH_2\text{-}NH_2 \;+\; Fe^{++}$$

$$C_6H_5\text{-}\overset{+}{C}H\text{-}CH_2\text{-}NH_2 \;+\; CH_3OH \longrightarrow C_6H_5\text{-}CH(OCH_3)\text{-}CH_2\text{-}NH_2 \;+\; H^+$$

Phenylacetylene,always with $FeCl_2$,yields the α-chlorophenylacetaldehyde:this aldehyde can arise from hydrolysis of the corresponding enamine:

$$C_6H_5\text{-}CCl{=}CH\text{-}NH_2 + H_2O \longrightarrow C_6H_5\text{-}CHCl\text{-}CHO + NH_3$$

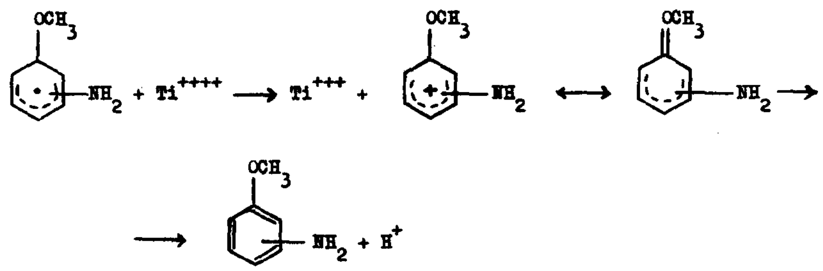
and,accordingly,it is also obtained from N-chloroamines under the same reaction conditions.

With the same reacting system (H_2NOSO_3H and $FeCl_2$ or $FeSO_4$) anisole gives in 38% yield a mixture of ortho and para anisidines whereas with toluene a mixture of ortho(37%),meta(21,5%) and para(41,5%) toluidines is obtained in 15% yield.Toluene had been previously[2] aminated by H_2NOSO_3H and $AlCl_3$ and the isomer distribution was:51% ortho,13% meta and 36% para.The larger amount of meta isomer obtained by the redox system is in accordance with the lower selectivity of a radical attack, even though the radical is a strongly electrophilic one,as the amino radical ion,$\cdot NH_3^+$.Under the same conditions with $FeSO_4$,meta-dimetoxybenzene afforded a basic product,87% of which was determined as 2,4-dimetoxyaniline and 13% as an uncharacterized amine,probably 2,6-dimethoxyaniline.All these reactions were carried out at room temperature (10-30°) in 95% methanol and the isomer distribution determined by gas-liquid chromatography.

Furthermore we have reinvestigated the $NH_2OH/TiCl_3$ redox system, already considered as source of amino radicals

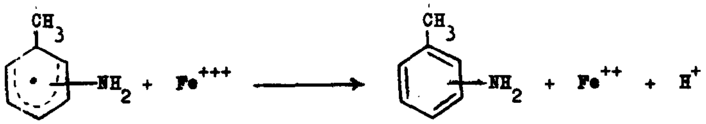
$$NH_2OH.HCl + Ti^{+++} \longrightarrow \cdot NH_2 + TiCl^{+++} + H_2O$$

by other Authors[3a,b,c],who succeeded in attacking aromatics such as benzene and toluene,but obtained instable basic products,probably arising from transformations,i.e.dimerization,of aminocyclohexadienyl radicals.In the case of an aromatic substratum such as anisole the resulting cyclohexadienyl radical intermediate should have been,in our opinion,more easily oxidizable and,in fact,we have obtained a mixture of ortho and para anisidines as the only basic product(yield:18%).The easier oxidability of this cyclohexadienyl radical could be explained by an electron transfer by Ti^{++++}, resulting in formation of a cation stabilized by resonance with the methoxy group(the same cation is involved in electrophilic substitutions):



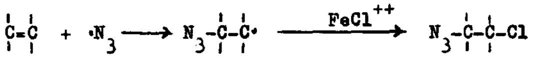
The reaction with NH_2OH and $TiCl_3$ would seem analogous to that of H_2NOSO_3H and ferrous salts,but the isomer distribution is quite different in the two cases(63% ortho,37% para with NH_2OH and34% ortho, 66% para with H_2NOSO_3H) and it is also different from that obtained in the reaction of N-chloropiperidine on anisole[4] (4% ortho and 96% para). The high selectivity observed in this last case was attributed by us to steric influence,which has now been confirmed by reduction of N-oxypiperidine with $TiCl_3$: in presence of anisole the isomer distribution is just the same obtained with N-chloropiperidine (4% ortho and 96%para). This isomer ratio does not change even if the reaction with NH_2OH is carried out in strong acidic medium in which a protonated amino radical should be present.

In an attempt to aminate toluene with NH_2OH in aqueous methanol we have added a $FeCl_3$ solution to the reaction mixture simultaneously to the addition of $TiCl_3$ solution. This expedient proved successful only partially since $FeCl_3$ is reduced by $TiCl_3$ faster than hydroxylamine, which on the other hand is not reduced by ferrous salts under these reaction conditions(10-30°C): the toluidines are in fact only the 40% of the basic product obtained in 14% yield. That is the ferric salt would be present in too little concentration for the complete oxidation of the cyclohexadienyl radical:



and, therefore, the isomer distribution (36% ortho, 18% meta, 46% para) is of little significance in this case, since the attack of the amino group on the aromatic ring is not followed by a sole reaction pathway.

Further information are provided by the reduction of NH_2OH with $FeCl_2$ in the presence of olefins: in boiling methanol we have obtained only the aminochlorination of the olefinic bond, even though in lower yields (10-15%) in comparison to the ones with H_2NOSO_3H. Once again both reactions, with NH_2OH and H_2NOSO_3H, seem to be identical, but their stereochemical course shows an important difference: in the case of cyclohexene, we have separated as benzoylderivatives the <u>cis</u> 1-amino-2-chlorocyclohexane with NH_2OH, and the corresponding <u>trans</u> isomer with H_2NOSO_3H. Both benzoylderivatives were already known[5] (<u>cis</u>: m.p. 153-4° and <u>trans</u>: m.p. 161-2°) and show notably different IR spectra. Actually the IR spectra of the raw benzoylderivatives show that the <u>cis</u> is the prevalent isomer with NH_2OH and the <u>trans</u> with H_2NOSO_3H, although they are always accompanied by smaller amount (not yet exactly determined) of the other isomer. In gas-liquid chromatography extensive decomposition of aminochloroderivatives occurs. The <u>trans</u> 1-amino-2-chlorocyclohexane is the prevalent isomer obtained also by reduction of 1-azido-2-chlorocyclohexane, arising from cyclohexene by a process showing the features of a radical addition[6]:



$$\text{C=C} + \cdot N_3 \longrightarrow N_3\text{-C-C}\cdot \xrightarrow{FeCl^{++}} N_3\text{-C-C-Cl}$$

In our opinion, also with the $NH_2OH/TiCl_3$ redox system in the presence of olefins aminochlorination should occur, to some extent, since, according to our results with N-chloroamines and $TiCl_3$, there is some evidence of an interaction like the following:

$$R\cdot + TiCl^{+++} \longrightarrow R\text{-}Cl + Ti^{+++}$$

Actually with cyclohexene we have found that the aminochloroderivative is always present together with the other compounds(cyclohexylamine and 2,2' diaminobicyclohexyle) already described by the Authors[3b,c] who previously investigated this redox system. Also in this case the 1-amino-2-chlorocyclohexane is mostly in the *cis* form.

Clearly NH_2OH and H_2NOSO_3H take part to the olefin chloroamination and amination of aromatics by means of different reacting species. On the other hand both redox systems show characteristic features of radical sources,like initiation of vinylpolymerisation[7] and exclusive formation of aminochloroderivatives with olefins in aqueos methanolic medium,that is against an alternative electrophilic addition. The prevalence of the *cis* isomer with NH_2OH makes us think of a coordinated addition of amino group and chloro atom to the double bond,but, owing to the incomplete stereospecificity and the initiation of vinylpolymerisation, the coordinated addition should be,to some extent, in equilibrium with an actual radical addition.

Researches are in progress to achieve further information about these seemingly very similar sources of amination,since the present results cannot be understood on the ground of a simple formulation of an amino radical in both redox systems.

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